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Modern Approaches in the Morphological Diagnosis of Inflammatory Bowel Diseases

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The purpose of the review: to summarize the main data of the literature and our own accumulated practical experience of everyday diagnosis of inflammatory bowel diseases (IBD) to better represent the morphological features and histological conclusions.
Key points. The microscopic picture of IBD is often represented by a combination of basic histological characteristics that can be detected in other diseases and only in rare cases can be considered pathognomonic. No single histological feature can be used in isolation to diagnose ulcerative colitis or Crohn's disease. Diagnostic accuracy is improved if several signs are taken into account at once, if changes within one or more parts of the intestine are analyzed, it is necessary to compare the identified changes with the clinical picture of the disease.
Conclusion. The presented stages of the morphological study of biopsy specimens in patients with IBD and the exact characteristics of the detected changes will help to increase the diagnostic value of the study of ileo- and colonobiopsies, as well as improve mutual understanding between gastroenterologists and pathologists and, as a result of interaction between specialists, will increase the accuracy of the diagnosis.
Keywords: inflammatory bowel disease, ulcerative colitis, Crohn's disease, pathological diagnostics

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Современные подходы в морфологической диагностике воспалительных заболеваний кишечника

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Цель обзора: обобщить основные данные литературы и собственный накопленный практический опыт каждодневной патолого-анатомической диагностики воспалительных заболеваний кишечника (ВЗК) для лучшего представления морфологических особенностей и гистологических заключений.
Основные положения. Микроскопическая картина ВЗК часто представлена сочетанием базовых гистологических характеристик, которые могут обнаруживаться при других заболеваниях и лишь в редких случаях могут считаться патогномоничными. Ни один отдельный гистологический признак нельзя использовать изолированно для постановки диагноза язвенного колита или болезни Крона. Диагностическая точность повышается, если учитываются сразу несколько признаков, если анализируются изменения в пределах одного или нескольких отделов кишки, обязательно сопоставление выявленных изменений с клинической картиной заболевания.
Заключение. Представленные этапы морфологического изучения биоптатов у больных с ВЗК и точная характеристика обнаруживаемых изменений помогут увеличить диагностическую ценность изучения илео-

и колонобиоптатов, а также улучшить взаимопонимание между гастроэнтерологами и патологоанатомами и как результат межколлегиального взаимодействия — повысят точность постановки диагноза.
Ключевые слова: воспалительные заболевания кишечника, язвенный колит, болезнь Крона, патолого-анатомическая диагностика

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Introduction

The incidence of chronic idiopathic inflammatory bowel disease (IBD) is steadily increasing worldwide and Russia is no exception in this trend [1–3]. This situation makes the histological diagnosis of IBD relevant for pathologists evaluating gastrointestinal (GI) biopsies. Reviews of the literature convincingly indicate that such a diagnosis cannot be made only on the basis of the results of histological examination and requires a clinical-pathomorphological approach [1–5]. To date, there are discrepancies in the designation and interpretation of changes detected in biopsy specimens. The purpose of this work is to summarize basic data of the literature and our own accumulated practical experience in the routine diagnosis of IBD. Particular attention is paid to the required minimum amount of clinical information and the accurate definition and designation of detectable pathological processes. Diagnostic categories that should be used in everyday practice are given.

Diagnosis of chronic idiopathic inflammatory bowel disease (IBD) is based on a close correlation between morphological changes, clinical features, endoscopic picture, results of visual diagnostic methods and laboratory data [1–5].

The microscopic picture, in fact, often consists of a combination of basic histological characteristics that can also be found in other diseases and can only rarely be considered pathognomonic [6–10]. Pathology diagnosis is of paramount importance in determining the choice of treatment, prognosis and follow-up [1–5].

The purpose of morphological diagnostics is to:

1. Distinguish IBD from other colitis.
2. Make a differential diagnosis between ulcerative colitis (UC) and Crohn's disease (CD).
3. Identify / exclude foci of dysplasia.

Clinical indications for biopsy

The "gold standard" for diagnosing IBD has not yet been determined. In fact, the diagnosis of IBD is based on a combination of anamnestic data, clinical evaluation, and typical endoscopic and histopathological features [6–10].

The main reason for referring the patient for endoscopic examination are the following symptoms: chronic diarrhea (loose stools lasting more than 4–6 weeks), hematochesia (blood in the stool), pain in the lower abdomen, mucous discharge from the rectum, the formation of fistulas, as well as unexplained systemic manifestations, such as fever and weight loss, or the presence of clinical signs that may reflect extraintestinal manifestations of IBD (joint, skin, eye, and others).

During a colonoscopy, it is important to assess the condition of the terminal parts of the ileum and take biopsy specimens from both unchanged and pathologically altered areas. Histological examination is mandatory for the diagnosis of IBD [1–5]. In chronic watery diarrhea with a normal endoscopic picture, biopsies are recommended for the diagnosis of microscopic colitis (lymphocytic or collagenous): two biopsy specimens from the ascending colon and sigmoid colon.

Clinical data

As mentioned earlier, clinical data are crucial for the correct interpretation of histopathological features. These data should always be submitted in the requisition form or in the form of a separate document with clinical data.

Sending a copy of the results of an endoscopic examination may be useful, but it in no way replaces the correct and complete preparation of a requisition form for pathology examination, which should include the conclusion of the endoscopist and gastroenterologist on a case-by-case basis. To confirm the microscopic picture and make a definitive pathology diagnosis, the pathologist needs to obtain detailed clinical and endoscopic data, especially in cases of newly diagnosed IBD. If detailed clinical information is not available, the diagnosis can only be descriptive.

The necessary accompanying information can be divided into the following categories:

1. Clinical history.

- Symptoms (features and duration): diarrhea, hematochezia, fever, etc.
- The presence of extraintestinal manifestations.

Current or previous therapy, with particular emphasis on drugs that may affect the intestinal mucosa, including specific therapy for IBD.

In all cases of referral of biopsy material, the medications taken by the patient should be reported. Recently, in the medical literature, there are more and more publications about drug associated colitis and an ever-expanding list of drugs that cause damage to the colon mucosa.

The time of the onset of the disease is extremely important. It is necessary to indicate the duration of the disease. It is reliably established that for the occurrence of diagnostic morphological manifestations of IBD, at least 4–6 weeks should pass, in some cases it may take one to two months [11].

2. Laboratory data.

It is advisable to present the results of current studies on intestinal infections and on parasites, the results of nonspecific inflammatory serological markers (ESR level and C-reactive protein), the results of tests for the presence of antineutrophil cytoplasmic antibodies (ANCA) and antibodies to *the Saccharomyces cerevisiae* (ASCAs)).

3. Endoscopic picture.

It is necessary to describe the main observed changes with an emphasis on continuous or segmental lesions.

If the changes are not visible endoscopically, then the chance of detecting them morphologically tends to zero. The exception is cases of microscopic colitis (lymphocytic or collagenous). If microscopic colitis is suspected, it is necessary to reflect this in the direction of a pathology examination and report the presence of watery diarrhea in the patient, medications taken, etc.

4. Data from other diagnostic methods.

It is necessary to provide information on other significant changes in the gastrointestinal tract, detected, for example, by ultrasound examination of the abdominal organs, CT enterography, and other methods.

Rules for taking biopsies

It has been shown that the diagnostic accuracy of pathology examination improves with an increase in the number of biopsies performed, including by taking biopsy specimens from various parts of the intestine [12]. Obtaining multiple biopsy specimens is important especially in the case of newly diagnosed IBD, whereas the number of biopsies may be reduced in subsequent examinations.

It should also be noted that CD is a transmural disease and therefore diagnosis by endoscopic biopsies has limitations and appears to be more difficult [13].

The optimal number of biopsy specimens for the primary diagnosis of IBD

Two biopsy specimens should be taken in the terminal part of the ileum, in the cecum, ascending, transverse and descending colon, sigmoid and rectum, even if the mucosa is not endoscopically changed.

Minimum number of biopsy specimens during follow-up

Two biopsy specimens should be taken from the affected parts of the colon and two biopsy specimens from the rectum. In the event of a discrepancy between the initial histological diagnosis and the clinical course during follow-up, be sure to repeat the complete sampling of the material (see earlier) to clarify the diagnosis. In addition, it is strongly recommended to revise the results of the previous histological examination.

Sampling to detect dysplasia in the long course of the disease (lasting more than 8–10 years)

This is a very controversial issue, since the requirements for the number of biopsy taken in the literature are high and are often ignored in everyday practice. The protocol essentially recommends two biopsies every 10 cm of colon, as well as biopsies from any suspicious areas of the colon mucosa.

Processing of biopsy specimens

Samples from each anatomical site should be adequate in size (the presence of a muscularis mucosa in the biopsy), carefully processed to avoid artifacts, immediately fixed in 10 % neutral buffered formalin and correctly labeled.

The diagnosis of IBD can be made in most cases using sections stained with hematoxylin and eosin. There is no gold standard rule regarding the number of histological sections on the slide to be examined, although it has been demonstrated that diagnostic accuracy increases with successive increases in the number of sections on the slide, especially with respect to the identification of granulomas in CD.

Particular attention should be paid to distinguishing “true lesions” from changes caused by preparation of the intestine for endoscopic examination and / or damage when taking a biopsy (Table 1) and from “minimal changes” that fall within the normal range of histological variability of the colon mucosa. Their accurate and unambiguous identification is necessary in order to avoid diagnostic errors.

Normal colon mucosa

The normal colon mucosa is characterized by a flat surface, parallel straight crypts of the same size, evenly distributed, less than 10 % of which may be slightly branching (Fig. 1), and the bottom of which reaches the muscularis mucosa.

The average normal number of crypts is 7–8 per millimeter of mucosal length, although this value may decrease in the cecum and distal rectum.

Irregular architecture is observed in the area of the location of lymphoid follicles, on the ileocecal valve and near the appendicular orifice.

The epithelium consists of absorbtive and goblet cells in the upper to middle third, where individual apoptous bodies can be observed, and immature cells in the lower third, where mitose figures can be found.

Paneth cells at the base of the crypts can be observed throughout the right colon (up to the hepatic flexure). Lymphocytes and plasma cells are usually present in the colon mucosa. They are more numerous in the cecum and show a decrease in density from the surface to the base.

Eosinophilic granulocytes are normally present in the colon mucosa, there are more of them in the right parts of the colon. Intraepithelial T-lymphocytes are present in the surface epithelium, normal is considered from the number of up to 20 lymphocytes / 100 enterocytes.

Lymphoid follicles can also be observed, having germinal centers and sometimes extending to the submucosa.

The main diagnostic histological signs

The diagnosis of IBD is based on the identification of a combination of basic histological characteristics (Table 2). They were described for a long time, but their sensitivity and specificity have not yet been established [6–10, 14].

Table 1. Changes caused by preparation of the intestine for endoscopic examination and / or trauma when taking a biopsy

· Desquamation of the epithelium · Acute hemorrhagic foci · Edema · Pseudolipomatosis · Reduction of intracellular mucus content · Increase in the number of mitoses · The presence of single neutrophils in the superficial epithelium, especially over lymphoid follicles, and in crypts (less than 1–2 neutrophils per crypt)

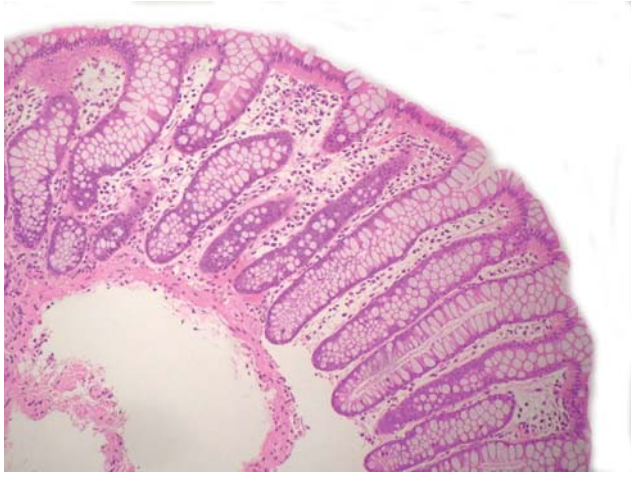

Fig. 1. Normal morphological characteristics of the colon mucosa. Magnification ×100. Staining H&E

1. Changes in the architecture of *the colon mucosa.*

1.1. Changes in the surface of *the colon mucosa.*

Loss of flat surface, manifested by slight unevenness or even pseudovilli surface (Fig. 2).

1.2. Deformation of crypts.

Loss of parallelism of crypts having variable diameter and shape, as well as irregular branching with dilatation up to cystic formation (Fig. 3).

1.3. Atrophy.

Reducing the size (Fig. 4) and the number of crypts (the distance between the crypts is greater than the diameter of one crypt) and / or shortening with an increase in the distance between the bottom of the crypt and the muscularis mucosa. This parameter should be evaluated in the absence of moderate / severe inflammation in the mucosa to avoid overestimation.

2. Inflammatory infiltration.

2.1. Neutrophilic.

The presence of neutrophilic leukocytes in the mucosa, superficial epithelium, epithelium of crypts (cryptitis) and lumen of crypts (crypt abscess) determines the activity of the disease (Figs. 5 and 6). Various schemes have been proposed in assessing the degree of activity, but their poor reproducibility limits their use in clinical practice [15–19].

2.2. Lymphoplasmocytic.

The increase number of plasma cells and lymphocytes in the mucosa that can be located focally or diffusely. This is an extremely important parameter, since the numerical range of lymphoid cells in the normal mucosa has not yet been clearly established in the literature. Therefore, its identification is reliable only when it comes to a noticeable increase.

2.3. Basal plasmacytosis.

The presence of a large number of plasma cells between the bottom of the crypts and the muscularis mucosa (Fig. 7).

2.4. Epithelioid granulomas.

Clusters of epithelioid cells (more than 5 histiocytes with a well-defined eosinophilic cytoplasm) sometimes in combination with multinucleated giant cells localized in the mucosa and / or in the submucosa (Fig. 8). They should not be confused with isolated giant multinucleated cells. 9) and cryptolytic granulomas, which can be detected around the destroyed crypts (Fig. 10).

3. 5. Increase in the number of lymphoid follicles.

The number of lymphoid follicles is within normal limits, when their number does not exceed two follicles per one millimeter of the colon mucosa.

4. Distructive changes.

4.1. Erosion.

Table 2. The main histological lesions in IBD

1. Changes in the architecture of the colon mucosa
1.1. Changes in the surface of the colon mucosa
1.2. Deformation of crypts
1.3. Atrophy
2. Inflammatory infiltration
2.1. Neutrophilic
2.2. Lymphoplasmocytic
2.3. Basal plasmacytosis
2.4. Epithelioid granulomas
2.5. Increase in the content of lymphoid follicles
3. Distructive changes
3.1. Erosion
3.2. Ulcers
3.3. Aphthous ulcers
4. Damage of the epithelium
4.1. Reducing in mucin content
4.2. Paneth cell metaplasia
4.3. Pseudopyloric metaplasia
4.4. Dysplasia/Intraepithelial neoplasia

A slight loss of superficial epithelium with mild inflammation in the absence of recognizable granulation tissue under it. They can be coated with exudate consisting of polymorphonuclear leukocytes, necrotic cells and fibrin (pseudomembranes).

4.2. Ulcers.

The lesion captures the entire thickness of the mucosa with the presence of granulation tissue at the base.

4.3. Aphthous ulcers.

Loss of superficial epithelium in the projection of the underlying lymphoid follicle.

5. Damage to the epithelium.

5.1. Reduction of mucin content.

Reducing the number of goblet cells and / or the content of mucus in them either in crypts or in the superficial epithelium.

5.2. Paneth cell metaplasia.

It consists of easily recognizable mature Paneth cells at the base of crypts and/or immature enterocytes containing typical supranuclear eosinophilic granules.

5.3. Pseudopyloric metaplasia.

Replacement of the epithelium of the crypts with glandular epithelium, resembling the antral glands of the stomach.

5.4. Dysplasia/intraepithelial neoplasia.

The term dysplasia is synonymous with intraepithelial neoplasia as recommended by the WHO definition. This term should not be used in the case of reparative and/or reactive changes.

Dysplasia is classified into low- and high-grade dysplasia, as in other parts of the gastrointestinal tract, according to structural changes such as the fusion of glands with cribrose and villous structures and *cytological characteristics* such as nuclear stratification, loss of cell polarity, pleomorphism, abnormal

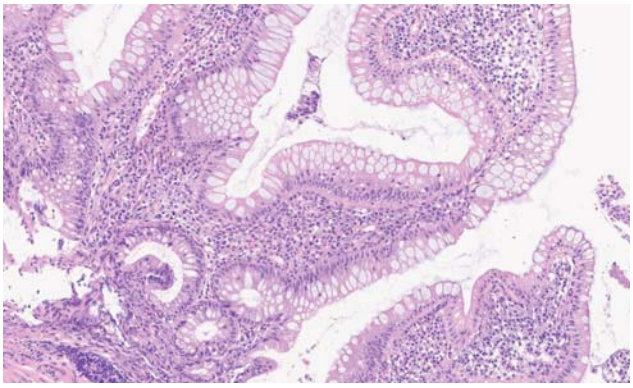

Fig. 2. Pseudovilli surface of the biopsy. Magnification ×200. Staining H&E

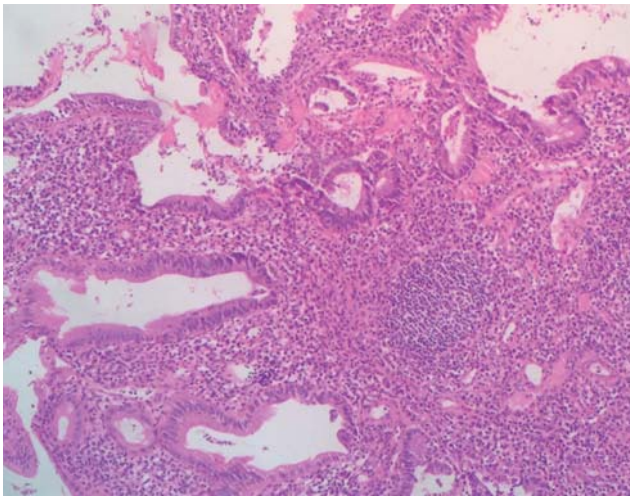

Fig. 3. Structural deformations of crypts. Magnification ×100. Staining H&E

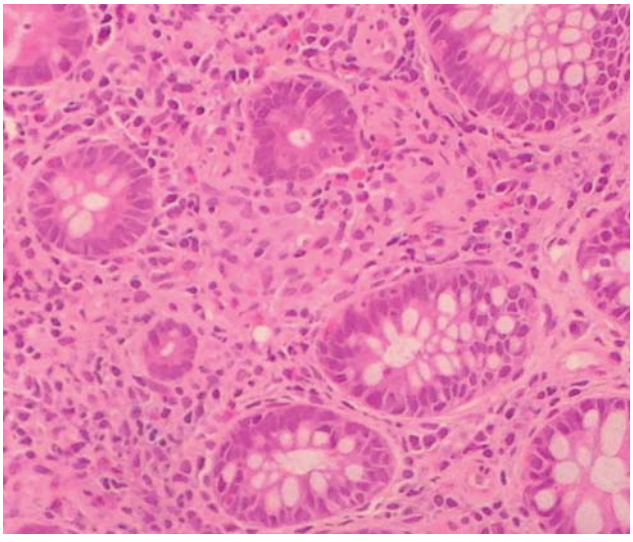

Fig. 4. Atrophy of crypts. Magnification ×300. Staining H&E

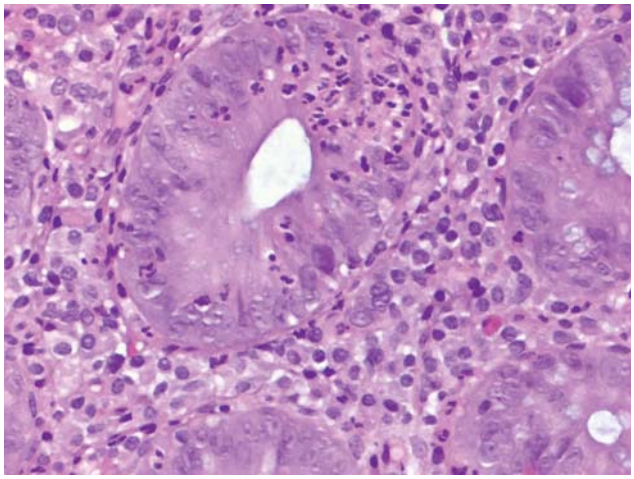

Fig. 5. Cryptitis. Magnification ×600. Staining H&E

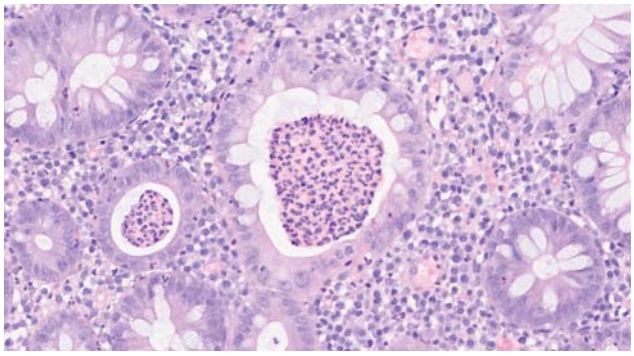

Fig. 6. Crypt abscesses. Magnification ×400. Staining H&E

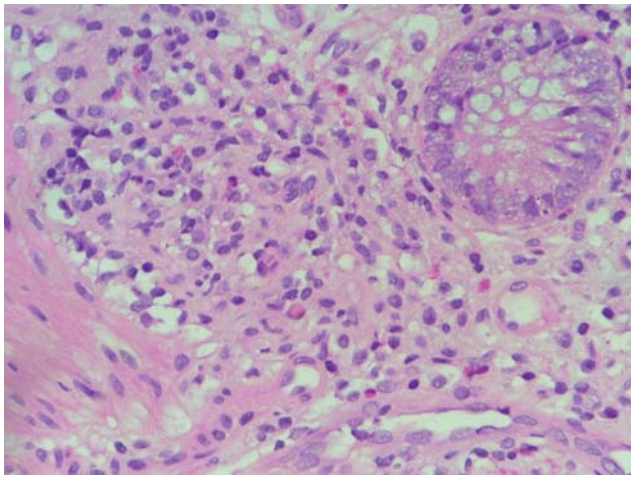

Fig. 7. Basal plasmacytosis. Magnification ×400. Staining H&E

nuclear-cytoplasmic ratio, nuclear hyperchromatism, an increase in the number and abnormal distribution of mitoses (the upper third of the crypts) and the presence of atypical mitoses. Dysplasia can occur from a flat mucosa and or in polypoid formations.

Polypoid lesions in IBD are characterized by different clinical risks. In accordance with the endoscopic description, when observing patients with IBD, the following are distinguished:

1) Dysplasia-associated lesion or mass (DALM): A raised lesion with dysplasia detected by colonoscopy. It is usually associated with an increased risk of developing or already having colorectal cancer.

2) Adenoma-like mass (ALM): A dysplastic lesion surrounded by a non-dysplastic mucosa is characterized by a risk of cancer as in sporadic adenomas.

There are no absolute histological diagnostic signs of IBD or any type of IBD. All diagnostic signs can only be more characteristic of one UC or for CD.

Diagnostic accuracy is improved if there are several signs, and not one, and also if the identified morphological changes correlate with the clinical picture of the disease. For example, a combination of diffuse violation of the structure of the crypts, the villous surface of the mucous membrane, atrophy of the crypts and basal plasmacytosis, especially if these changes are continuous and increase in the distal regions, are highly likely for UC, while the segmental nature of inflammation and focal changes in the structure of crypts in combination with non-cryptolytic granulomas suggest CD.

If the above diagnostic signs do not allow for a differential diagnosis between UC and CD, the diagnosis is formulated as non-classified IBD [20, 21].

The severity of the pathological process may be important. Thus, severe structural changes in crypts are more characteristic of UC than of CD, while focal and not so significant damage to crypts does not have a differential diagnostic value.

The traits commonly used to differentiate IBD from infectious colitis, or other “non-IBD” colitis , and to differentiate UC from CD, are summarized in Tables 3, 4, and 5.

Examination of biopsy specimens from the ileum and upper gastrointestinal tract

Examination of biopsy specimens from the ileum in IBD

Most patients with CD have pathological changes in the mucosa of the terminal parts of the ileum. There is a disorder of the architecture of the villi and crypts, local or focal inflammation, erosion and pyloric metaplasia. Granulomas and giant cells are

rare, but they are important in conducting a differential diagnosis between CD and UC [22].

In some cases of UC, there is inflammation of the distal parts of the ileum. Despite the fact that this is considered as retrograde ileitis, involvement of the cecum is not always observed.

The main results of the ileum biopsies in IBD are:

- In IBD, inflammation of the ileum is with asignificant argument against ulcerative colitis and testifies in favor of CD;
- Non-cryptolytic granulomas in biopsy specimens from the affected mucosa of the ileum can distinguish CD from UC.

Study of biopsies from the upper gastrointestinal tract in IBD

Inflammation of the upper gastrointestinal tract is characteristic of CD and is quite rare in UC. Involvement of the upper gastrointestinal tract in the pathological process is more characteristic of children than of adults [23].

Granulomas in gastric biopsy specimens can be observed in 0–83 % of cases of CD, depending on the published results of studies [24]. Granulomas from any part of the gastrointestinal tract are convincing evidence in favor of CD and against UC. However, in themselves, they do not allow to diagnose CD, since they can occur in other clinical situations.

With CD, the duodenum is often involved in the process, but this phenomenon can occasionally be observed in UC too [25]. In this situation, diffuse chronic inflammation and crypt changes similar to those in the colon may be observed.

Focal active gastritis, which is characterized by focal mixed perifoveolar or periglandular inflammatory infiltrate with epithelial damage, is known as a sign of CD (Fig. 11) [23–25]. Even if it is known that the patient suffers from IBD, *Helicobacter pylori* infection should always be ruled out.

Involvement of the esophagus in the pathological process can be established if granulomas are detected. In CD, lymphocytic esophagitis is also described.

The main recommendations based on the results of the assessment of biopsies from the upper gastrointestinal tract in IBD:

- Involvement of the upper gastrointestinal tract in CD is much more common than in UC;
- Before including in the diagnosis of IBD the involvement of the upper gastrointestinal tract in the pathological process, other common causes should be excluded, in particular, GERD and *Helicobacter pylori* gastritis;
- The detection of granulomas in biopsy specimens from the upper gastrointestinal tract increases the confidence of the diagnosis of CD.

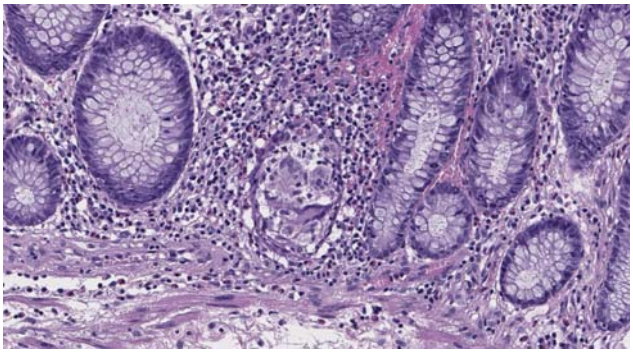

Fig. 8. Epithelioid-cell granuloma. Magnification ×200. Staining H&E

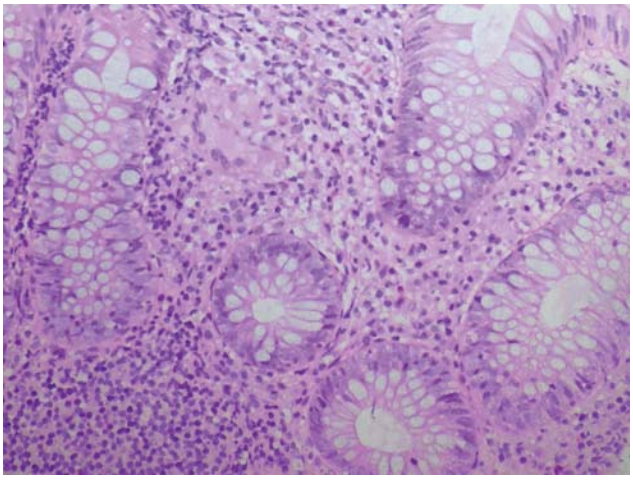

Fig. 9. Giant multinucleated cell. Magnification ×400. Staining H&E

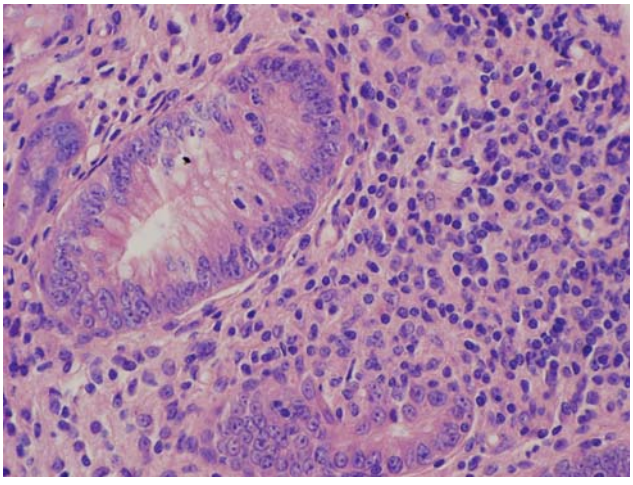

Fig. 10. Cryptolytic granuloma. Magnification ×400. Staining H&E

Table 3. Morphological characteristics for diagnostics and classification of IBD

Characteristic	IBD > infectious colitis	Infectious colitis > IBD	UC > CD	CD > UC
Structural characteristics				
Preservation of the normal structure architecture		+++		+
Crypt deformation	+++		++	
Crypt atrophy	+++		++	
Diffuse character of the crypts change			+++	
Focal changes in crypts				+
Irregular mucosal surface	+++		++	
Inflammation				
Basal plasmacytosis		+++		
Lymphoid aggregates		++		
Diffuse chronic inflammation			+++	
Focal chronic inflammation				++
Inflammation in the upper mucosa		+		
Granulomas (not cryptolytic)	++			++++
Acute inflammation		+		
Widespread cryptitis			+	
Other changes				
Reduction of mucus content			++	
Paneth cell metaplasia	+			
Ileitis				++

Note: CD — Crohn's disease; UC — ulcerative colitis. + weakly distinctive; ++ moderately distinctive; ; +++ very distinctive; ++++ is the most distinguishing feature.

Table 4. Morphological characteristics in favor of ulcerative colitis

Credibility	Morphological characteristics
The most significant	Diffuse structural disorders of the crypts both within the same compartment of the intestine and between compartments
	Diffuse anomalies of the crypts inside the intestine
	Crypt atrophy
	Anomalous crypt architecture
	Villous or uneven mucosal surface
	Reduced mucus content in the epithelium
	No inflammation of the ileum
Less reliable	Widespread cryptitis
	Increasing changes in the distal parts; diffuse nature of the inflammatory infiltrate; diffuse structural changes in crypts

Table 5. Morphological characteristics suggestive of Crohn's disease

Reliability	Features
The most significant	Granuloma (non-cryptolytic)
	Focal or focal chronic inflammation
	Focal or segmental deformity of the crypts
	Ileal bowel injury
Sufficiently reliable	Absence of a proximal-distal gradient of changes
Not very reliable*	Disproportionate inflammation in the submucosa
	Individual crypt abscesses
	Focal cryptitis

Note: * Evidence is conflicting or scarce. Focal cryptitis, in particular, can be found in many situations, including ulcerative colitis and infectious colitis.

Practical diagnostic algorithm

Pathological diagnosis of IBD is an extremely difficult task and, unfortunately, in most cases it cannot be performed quickly and easily, but, on the contrary, requires patience, time and the ability to recognize errors [26–28].

The sequence of the diagnostic process can be summarized as follows:

- Identification of intestinal biopsy specimens with normal mucosal characteristics.
- Identification of morphological changes in a single affected part of the intestine, which are different in their characteristics.
- Definition of the disease as focal or diffuse (in a specific individual biopsy and within the same anatomical part of the intestine).
- Definition of the disease as continuous or segmental (the presence of preserved areas).
- Definition of a disease with a predominant lesion of the left or right half of the colon.
- Evaluation of the ileum and biopsy specimens from the upper gastrointestinal tract.
- Formulation of the diagnostic hypothesis.
- Evaluation of the correspondence between this hypothesis and clinical data.
- Possible obtaining additional clinical data.
- Revision of previous biopsies is possible.
- Final diagnostic conclusion.

Diagnostic categories

1. Diagnostic.

This category should only be used for adequate biopsies, complete clinical data, a typical histological picture, and its consistency with clinical data. In fact, it is important to emphasize that an erroneous positive diagnosis can lead to long-term unjustified treatment and requirements for patient adherence to strict follow-up protocols with high socioeconomic costs. Conversely, an erroneous negative diagnosis leads to the persistence of symptoms or their rapid recurrence, which leads to the need for a second examination of the patient. As a rule, the correct diagnosis is made later, and the patient has an increased risk of possible complications.

2. Extremely suspicious of UC or BC.

This category should be used when typical histological features are combined with improper and/or incomplete biopsy collection and/or insufficient clinical data and/or clinical-pathological mismatch.

3. IBD unclassified.

This term should be used only in the case of incomplete collection of biopsy specimens and a small amount of clinical data or their complete absence. This diagnosis is based on a histopathological picture, which does not allow for a differential diagnosis between UC and CD. It should be used in a limited number of cases. In most of them, this should be a temporary diagnosis, which will be clarified by subsequent histological examinations with the correct taking and a sufficient number of biopsies and with detailed accompanying clinical information confirming the diagnosis.

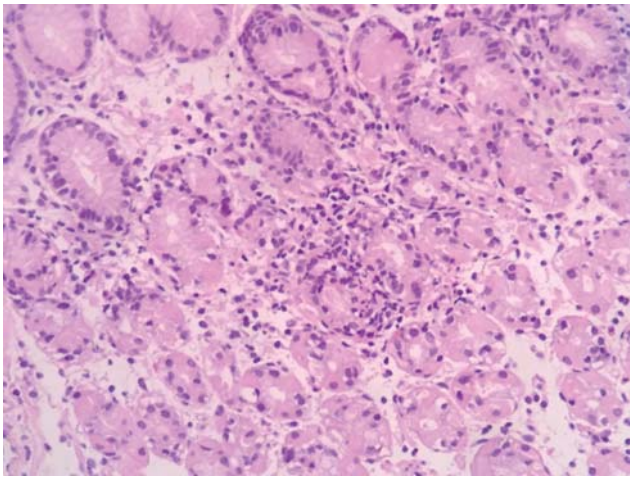

Fig. 11. Focal active gastritis. Magnification ×100. Staining H&E

4. IBD in remission.

This term should never be used as a diagnostic term and should always be accompanied by the statement “extremely likely”. The histological picture, in fact, is not specific and can be observed in other diseases: therefore, this diagnosis should be made only in the presence of previous diagnostic histological biopsies with confirmed active disease.

Diagnostic categories to avoid

1. Undetermined colitis.

Initially, the term was proposed for surgical material showing a histological picture typical of both UC and CD, and later it was incorrectly used in the same sense for the diagnosis of biopsy material. In cases of biopsy diagnosis, in contrast, the term “chronic idiopathic inflammatory bowel disease” (IBD unclassified) should be used.

2. Chronic colitis.

This term has no diagnostic meaning, since it does not identify any clinical and pathological nosology and, therefore, is completely devoid of any clinical value. Its use in the study of biopsy and surgical material should be completely excluded.

Making conclusion

Depending on the achieved level of diagnostic reliability, three different versions of the conclusions and its components can be distinguished.

1. Final morphological diagnosis.

- Histopathological description (although histopathological description may seem superfluous, it may be useful in subsequent studies to assess the "level of certainty", even if slides are not available, and it is strongly recommended especially in cases where the diagnosis is not conclusive).

- Variant of IBD: UC, CD or chronic idiopathic inflammatory bowel disease IBD unclassified.

- Assessment of disease activity.

- Evaluation of dysplasia.

2. The diagnosis is presumptive (most likely).

- Histopathological description.

- Statement assessing the subjective degree of probability of confirming the diagnosis: Suspicious, more or less likely UC, CD or chronic idiopathic inflammatory bowel disease (IBD unclassified).

- Activity assessment.

- Evaluation of dysplasia.

- Comments explaining the reasons that prevent a definitive diagnosis (the volume and nature of the biopsy specimens and/or insufficient clinical data).

3. Descriptive diagnosis

A simple description of the histological picture should be used only for cases that demonstrate obvious pathological changes, which, however, do not correspond to any particular nosology. The use of such an approach in the form of a descriptive conclusion should be limited to cases where the pathologist wants to report the presence of a pathology that requires further diagnostic search.

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